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Background

The clinical benefit of Therapeutic Drug Monitoring (TDM) of mycophenolate mofetil (MMF) when used in children with lupus (SLE) has been scarcely studied.

Aim

(i) To model mycophenolic acid (MPA; the active moiety of MMF) pharmacokinetic profiles (PK); (ii) to explore the relationships between exposure indices to MPA and the clinical status.in paediatric inpatients with SLE receiving a maintenance immunosuppressive therapy including MMF.

Methods

We launched a non-interventional study with analysis of clinical, biological and pharmacokinetic information. Full-PK profiles of MPA were modelled using an iterative two-stage approach (1). The clinical status was defined by the SLEDAI, the SLE being considered active for a score ≥6. Relationships between MPA through concentrations (C_0), AUC (Area Under Curve) or AUC/dose values, and the disease's activity were studied using logistic regression analysis.

Results

Twenty six children (aged 10 to 17) with SLEDAI score from 0 to 20 (median: 4) followed-up in 5 French centres were included. High PK interpatient variability was observed: $AUC_{0\text{-}12h}$=40.51±20.49 mg.h/L. Trough concentrations (C_0) were poorly correlated to the global exposure to MPA (AUC). Multivariate analysis reported: (i) no relationship between C_0 and SLEDAI; (ii) patients with an $AUC_{0\text{-}12h}$/dose <0.058 h/L were more likely to have an active disease (OR=4.8; 95CI: 0.9-25.0; p=0.067).

Conclusion

A tendency to a relationship between the lupus activity and the global MPA exposure was observed. Further data are needed to develop PK tools that could estimate the AUC using a limited sampling strategy and to lead prospective trials testing the clinical impact of a MMF TDM based on the AUC.

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